



MEDICAL UNIVERSITY OF WARSAW

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STATYSTICAL ANALYSIS PLAN

14/01/2020

Prophylactic Use of Dural Tenting Sutures in Elective Craniotomies – Is It Necessary? A multicenter Randomised Study.

1. ADMINISTRATIVE INFORMATION

Title:

Prophylactic Use of Dural Tenting Sutures in Elective Craniotomies – Is It Necessary? A multicenter Randomised Study. Statistical Analysis Plan

Trial registration:

ClinicalTrials.gov Identifier: NCT03658941

SAP version and date:

1.3, 11.09.2018

Protocol version reference:

12.09.2018

SAP revision history, justification and timing:

Roles and responsibility:

Zbigniew Lewandowski
Senior statistician responsible
Department of Epidemiology and Biostatistics, Medical University of Warsaw, Poland

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2. INTRODUCTION

Background and rationale:

This study evaluates the necessity of dural tenting sutures in craniotomies. The sutures elevate the dura, a layer between the brain and skull. Supposedly, by doing so, they prevent blood collecting between dura mater and the skull. These blood collections, called epidural hematomas, contributed greatly to postoperative mortality in the early days of neurosurgery. There have been several reports questioning the ongoing need for them in neurosurgery, thanks to modern hemostatic techniques. Moreover, it has been published in the literature, and is a common knowledge as well, that some neurosurgeons do not use these sutures at all, and do not have worse outcomes than their colleagues.

In this study, half of the randomly assigned participants will undergo craniotomy without dural tenting sutures and will be considered an intervention group. The other half will undergo craniotomy with these sutures.

Objectives:

To evaluate the necessity of dural tenting sutures in elective supratentorial craniotomies in adults.

3. STUDY METHOD

Trial design:

Parallel group, 2 arms, allocation ratio 1:1

Intervention 1: no dural tenting sutures

Active control group: dural tenting sutures

Randomization

The randomization will be performed in 1:1 proportion

Sample size: The following assumptions were made:

Sample size calculation was made using calculator available on-line (Sealed Envelope Ltd. 2012. Power calculator for binary outcome non-inferiority trial. [Online] Available from: <https://www.sealedenvelope.com/power/binary-noninferior/> [Accessed Mon Sep 23 2019]). Initially, alpha level of 0.05, power (1-beta) 90%, 0.7 % EDH occurrence in the experimental group, while in control group expected frequency of 1.4 % was assumed. Non-inferiority limit, d, was set on 0.7 %. The study aims to include 908 patients in every study group, 1816 patients in total. Because a loss of about 10% (181.6) of patients is expected due to nonadherence of the surgeons to the allocation and rounding up by 2.4, 1000 patients will be included in each group, 2000 patients in total. However, the risk of extradural haematoma may be evaluated more accurately after a systematic review is prepared regarding the necessity of dural tenting sutures, resulting in possible change of sample size.

Framework:

Noninferiority study

Hypothesis: The risk of formation of epidural hemorrhage is not higher without dural tenting sutures

Statistical interim analyses and stopping guidance:

After enrollment 100 participants

Date of interim analysis:

Anticipated 31.01.2019

Interim analysis:

- 1. Reoperation due to epidural hematoma**
- 2. Postoperative 30-day mortality**

Planned adjustment of the significance level due to interim analysis:

High power of the analysis of 95%.

Details of guidelines for stopping the trial early:

Primary outcome and secondary outcome significantly higher in an intervention group.

Bioethics committee decision to discontinue the study.

Timing of final analysis:

September 1, 2021 – April 1, 2022

Timing of outcome assessments:

Postoperative 30-day mortality: October 1, 2021 – December 31, 2021

Rest of the outcomes will be assessed during hospitalization of the subject.

4. STATYSTICAL PRINCIPLES

Confidence intervals and P values:

95% CI and 0.05 for alfa level

Description of multiplicity:

not applicable

Level of statistical significance:

0.05

Confidence intervals to be reported

95%

Adherence and protocol deviations:

Definition of adherence to the intervention (and how this is assessed):

It will not be assessed until the blinding is broken (during interim analysis or at the end of the study).

Presentation of adherence:

With the data reported shortly after the surgery with the information about number and type of dural tenting sutures (in control group) or lack of dural tenting sutures (in intervention group).

Analysis populations:

1000 patients in control and intervention group

5. ANALYSIS

Outcome definitions:

Outcome 1:

Primary Outcome Measure:

Title:

Reoperation due to epidural hematoma

Description:

Percentage

Time Frame:

During hospitalization for the surgery, approximately 2 days postoperatively

Outcome 2:

Secondary Outcome Measure:

Title:

Postoperative 30-day mortality

Description:

Percentage

Time Frame:

30-day postoperatively

Outcome 3:

Secondary Outcome Measure:

Title:

Postoperative 30-day readmission to a neurosurgical or neurological department

Description:

Percentage

Time Frame:

30-day postoperatively

Outcome 4:

Secondary Outcome Measure:

Title:

New neurologic deficit or deterioration of a previous one as evaluated on a 7-10 postoperative day.

Description:

Specific description of a neurologic deficit

Time Frame:

During hospitalization, approximately 7-10 days postoperatively

Outcome 5:

Secondary Outcome Measure:

Title:

Cerebrospinal fluid leak requiring treatment

Description:

Percentage

Time Frame:

During hospitalization, approximately 7-10 days postoperatively

Outcome 6:

Secondary Outcome Measure:

Title:

Deterioration of postoperative headaches over 5 in Numerical Rating Scale

Description:

The Numeric Rating Scale is an 11-point scale for patient self-reporting of pain. 0 represents no pain, 10 – the worst possible pain.

Time Frame:

During hospitalization, approximately 7-10 days postoperatively

Outcome 7:

Secondary Outcome Measure:

Title:

Epidural collection volume over 10 ml measured radiographically

Description:

The volume of the epidural collection measured in a postoperative CT scan

Time Frame:

During hospitalization, approximately 1-3 days postoperatively

Outcome 8:

Secondary Outcome Measure:

Title:

Epidural collection thickness over 3 mm measured radiographically

Description:

The thickness of the epidural collection measured in a postoperative CT scan

Time Frame:

During hospitalization, approximately 1-3 days postoperatively

Outcome 9:

Secondary Outcome Measure:

Title:

Midline shift over 5 mm

Description:

Midline shift caused by the epidural collection measured in a postoperative CT scan

Time Frame:

During hospitalization, approximately 1-3 days postoperatively

Analysis methods:

Relative risk will be applied to examine primary outcome.

Missing data:

In order to show the possible impact of the lack of data on the results, two types of analyzes: intention to treat and per protocol will be performed.

Additional analyses:

It is planned to perform analysis for subgroup of patients with a size of a craniotomy at least of 8 cm.

Harms:

Lack of baseline data due to incomplete documentation

Statistical software:

Procedures of SAS System 9.4.